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Use of radiotracer labeling of pulmonary nodules to facilitate excisional biopsy and metastasectomy in children with solid tumors☆

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ABSTRACT

Purpose: Excision of suspected pulmonary metastases in children is challenging in the setting of multiple nodules or nodules that are small, deep, or soft. This study describes preoperative technetium macro-aggregated albumin (Tc 99m MAA) localization of pulmonary lesions to aid in intraoperative identification and resection.
Methods: Patients with past or present pediatric solid tumors who underwent resection of pulmonary nodules following CT-guided Tc 99m MAA labeling were identified. The primary outcomes were successful preoperative localization and subsequent resection.
Results: Metastasectomy following Tc 99m MAA localization was performed 15 times in 11 patients from 2014 to 2016. Mean age was 13 years; the most common diagnosis was osteosarcoma (33%). Tc 99m MAA labeling was attempted in 24 nodules with mean nodule diameter 6 ± 5 mm and mean depth from the pleural surface of 12 ± 17 mm; localization was successful in 23 nodules (96%). Subsequent resection was performed by thoracotomy in 12 cases and thoracoscopy in 3. All labeled nodules were identified intraoperatively; two were not resected and 17 of the 21 nodules resected demonstrated metastatic disease on pathology.
Conclusion: Tc 99m MAA labeling of pulmonary nodules in children is effective in facilitating resection of subcentimeter intraparenchymal metastases identified on preoperative imaging. Furthermore, this technique allows for thoracoscopic metastasectomy in select patients.
Type of study/level of evidence: Case Series/Level IV.

The most common location for metastases in children with pediatric solid tumors is the lung [1]. While some metastatic tumors including osteosarcoma benefit from aggressive metastasectomy, others are treated with chemotherapy or radiation [2–4]. Nonetheless surgical excision of nodules identified on surveillance imaging is typically needed to confirm the diagnosis. Studies have shown even nodules less than 5 mm should be investigated due to risk of malignancy [5]. Whether performed for diagnostic or therapeutic purposes, excision of suspected metastatic nodules can be challenging due to small size or deep location. For tumors such as osteosarcoma, additional lesions not identified on preoperative imaging are often found at thoracotomy [6]. Incomplete metastasectomy can occur if these unexpected nodules are taken in place of those identified on CT. Finally, tumors that have a softer consistency can be difficult to palpate intraoperatively.

Preoperative localization of such nodules in children has been described using blue dye, microcoil, or wire and hook techniques [7–9]. These methods have limitations including diffusion of blue dye and dislodgement of physical markers; thus, dual localization approaches in children have also been described [10,11].

Radiotracer labeling using technetium macro-aggregated albumin (Tc 99m MAA) has been shown to be safe and effective in aiding with thoracoscopic resection of indeterminate pulmonary nodules in adults [12–15]. It has not been described, however, for use in resection of suspected pulmonary metastases in children. The purpose of this study was to describe our center's experience with preoperative Tc 99m MAA labeling for thoracoscopic or open resection of lung nodules in children with a history of solid tumors and suspected metastatic disease. We hypothesized Tc 99m MAA labeling would be safe in children and facilitate both excisional biopsy and complete metastasectomy.

1. Methods

A retrospective review of patients with known pediatric malignancies who underwent thoracoscopic or open resection of suspicious

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pulmonary nodules following CT-guided Tc 99m MAA labeling was performed after institutional review board approval was obtained. Tc 99m MAA labeling was utilized in patients with suspected pulmonary metastases when intraoperative identification of nodules was anticipated to be challenging due to preoperative imaging features including size and depth. This method of preoperative localization was incorporated into the pediatric surgical practice at our institution following successful utilization of the technique described by Stiles et al. in adult populations [13]. Patients were 21 years of age or less at operation and all included patients underwent pulmonary resection between February, 2014 and January, 2017.

Patient information including demographics, oncologic history, preoperative imaging features, operative details, and outcomes including pathology of resected nodules was retrospectively reviewed. Size of Tc 99m MAA labeled nodules and their depth from the pleural surface on CT were recorded in millimeters (mm). Descriptive statistics were performed; continuous variables were reported as mean (standard deviation) and categorical variables as *n* (%). The primary study outcomes were 1) successful pre-operative Tc 99m MAA localization and 2) intraoperative identification and resection following localization. Secondary outcomes included safety of Tc 99m MAA localization, intraoperative identification of nodules not visualized on preoperative imaging, and utilization of thoracoscopic resection following Tc 99m MAA labeling.

1.1. Tc 99m MAA labeling technique

The labeling procedure was performed in the Radiology suite on the morning of the lung resection operation after the radiologist and surgeon determined the lung nodules to be localized. Conscious sedation or general anesthesia was used depending on patient age and those who received general anesthesia were transported directly from the Radiology suite to the operating room. The specific technique for Tc 99m MAA labeling has been described by Stiles et al. [13] Briefly, a 19 to 25-gauge coaxial needle was introduced under CT guidance (without intravenous contrast) through the chest wall and advanced to the pulmonary nodules of interest (Fig. 1). Needle size varied based on patient age and size. After the tip of the needle was confirmed by CT to be at or adjacent to the nodule, approximately 0.3 mCi of Tc 99m MAA (0.1 mL) was injected. Immediate planar scintigraphy was performed to confirm presence of the Tc 99m MAA radiotracer in the thorax (Fig. 2). Post-procedure pneumothorax was assessed by CT. Enlarging or symptomatic pneumothoraces resulted in chest tube placement in the Radiology suite under imaging guidance. Stable, asymptomatic pneumothoraces were observed. CT images from radiotracer injection are immediately available electronically for the surgeon to review in the operating room and guide use of the radioprobe.

1.2. Operative technique

Patients underwent thoracoscopy or thoracotomy based on history of lung resections, oncologic diagnosis, and surgeon preferences. Approach was determined at the preoperative clinic visit by the pediatric surgeon and patient. Thoracotomy was performed in patients with a history of osteosarcoma so that palpation could be performed to identify potential metastases not seen on imaging. For patients who underwent thoracotomy, a standard anterolateral thoracotomy was performed after double-lumen endotracheal tube intubation. A sterile gamma radioprobe (Daniel Lung Probe, Dilon Diagnostics, Newport News, VA) is passed over parenchyma to identify the lung parenchyma with maximum signal, which was resected using staplers. Since the radiotracer used is bound to a large molecule (macro-aggregated albumin) there is little diffusion away from the site of injection. The signal diminishes substantially within mm from the injected site. Any additional nodules identified by visualization or palpation were also resected and sent for frozen section and permanent pathologic analysis. Lobectomies were performed for central nodules in close proximity to lobar vasculature or bronchi on a case by case basis. For patients with bilateral nodules localized, sequential thoracotomies were performed under the same anesthetic by completing one side then repositioning the patient for the other side.

Thoracoscopic resection was initiated by placing a 5 mm camera port for initial inspection. Based on findings, additional ports were placed including a 10 mm port for introduction of a sterile gamma radioprobe and subsequent resection after identification of labeled nodules or a thoracotomy was performed. Port placement was determined on a case by case basis due to varied anticipated location of nodules. Thoracoscopic wedge resection was performed using staplers with guidance of the radioprobe to ensure precise resection of the affected area. The radioprobe was then reintroduced to confirm there was minimal remaining signal in the pulmonary parenchyma. Wedge resection was also performed for any non-labeled nodules identified by thoracoscopic exploration. All resected tissue was sent for frozen section and permanent pathologic analysis. A chest tube was placed on the operative side for all patients.

2. Results

Lung resection aided by preoperative Tc 99m MAA localization was performed 15 times in 11 patients during the study period (Table 1); two patients underwent multiple metastasectomies during the study period. Five patients overall (46%) had a history of previous thoracotomy. Four patients (33%) had a history of osteosarcoma. Other preexisting oncologic diagnoses included Wilms tumor, Ewing

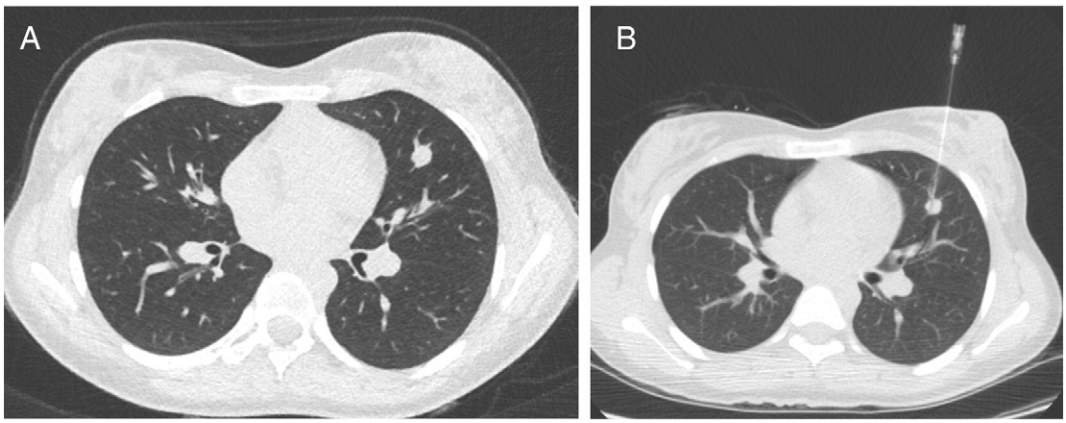

Fig. 1. Pre-operative CT demonstrating a suspicious nodule in the lingula (A) that was subsequently injected with Tc 99m MAA under CT guidance (B).

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